

ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, lymphoma, or carcinoma.

199. (New) The mammalian cell of Claim 195, wherein said mammalian cell is derived from or is contained in a human, non-human primate, mouse, rat, gerbil, hamster, or rabbit.

200. (New) A mammalian cell containing the HSV-1-derived vector of any of Claims 185, 186, 187, 189, 190, 191, 193, or 194, or unpackaged DNA thereof.

201. (New) A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing an HSV-1-derived vector selected from the group consisting of Prom Δ LAT Δ 34.5 and Prom Δ LAT Δ 34.5-GFP, or containing a derivative of any of these.

202. (New) A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of any of Claims 185, 186, 187, 189, 190, 191, 193, or 194.--.

REMARKS

Applicant's Preliminary Amendment is submitted together with a divisional application directed to Claims 120-178, originally filed in pending parent U.S. Serial No. 09/299,817, which claims were designated Group IV in a restriction requirement, mailed August 1, 2000.

The amendment of the title (at page 1, line 1) and in the Abstract of the Disclosures (at page 45, line 2), is to bring these into conformity with the new claims 185-202, and no new matter is introduced.

Applicant believes that no new matter is introduced by any amendments made herein.


At page 1, line 4, Applicant has added continuing data explaining the relationship to U.S. Serial No. 09/299,817. Please cancel Claims 1-119 and 179-184, without prejudice, as being directed to designated claim Groups I, II, and III. Please cancel Claims 120-178, without prejudice, and add new Claims 185-202.

The cancellation of Claims 1-119 and 179-184, without prejudice, is made because Claims 1-119 and 179-184 were designated claim Groups I, II, and III, and are not directed to the elected subject matter of the present division (i.e., Group IV).

Applicant's cancellation of Claims 120-178 is made without prejudice. New Claims 185-202 are added, and support is found, for example, in Claims 120-178, as originally filed.

In view of the above amendments and remarks, it is submitted that this application is now ready for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney at (213) 896-6665.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

In the Title, at page 1, lines 1-2, please delete "A HERPES SIMPLEX VIRUS TYPE 1 (HSV-1)-DERIVED VECTOR FOR SELECTIVELY INHIBITING MALIGNANT CELLS AND METHODS FOR ITS USE TO TREAT CANCERS AND TO EXPRESS DESIRED TRAITS IN MALIGNANT AND NON-MALIGNANT MAMMALIAN CELLS", and insert therefor:

--A HERPES SIMPLEX VIRUS TYPE 1 (HSV-1)-DERIVED VECTOR FOR SELECTIVELY INHIBITING MALIGNANT CELLS AND [METHODS FOR ITS USE TO TREAT CANCERS AND TO EXPRESS] FOR EXPRESSING DESIRED TRAITS IN MALIGNANT AND NON-MALIGNANT MAMMALIAN CELLS--.

At page 1, line 4, before "Background of the Invention", please insert the following:

--This application is a division of U.S. Serial No. 09/299,817, filed on April 26, 1999.--.

In the Abstract, beginning at page 45, line 2, please delete the entire paragraph, and insert therefor the following:

--[Disclosed is a method of selectively inhibiting the growth of malignant cells in mammals, including humans. The method selectively inhibits the growth of malignant cells of all varieties, and is particularly useful in treating brain tumors and other malignancies of the central nervous system. The method employs HSV-1-derived vectors containing a DNA having a deletion in both copies of the LAT gene and both copies of the ICP34.5 gene of HSV-1. The vectors are delivered to malignant cells either in vivo or in vitro, in accordance with the method.] Disclosed is an HSV-1-derived vector containing a DNA having a functional LAT promoter, or operative fragment thereof, a deletion in both copies of the HSV-1 LAT gene, and a deletion in both copies of the HSV ICP34.5 gene. The HSV-1-derived vectors are non-neurovirulent and do not spontaneously reactivate from latency, and they optionally contain a functional HSV thymidine kinase gene, which can enhance the

effectiveness against cancer of drug treatment with gancyclovir or acyclovir. Alternatively, the HSV-1-derived vectors contain at least one transcriptional unit of a LAT promoter sequence operatively linked to a nucleic acid encoding a preselected protein. In some embodiments, the preselected protein is a nucleotide sequence encoding a polypeptide toxic for cells expressing the vector, for example, human interferon- γ . [A method of expressing in a mammalian cell a gene encoding a preselected protein, a method of treating a genetic defect, and a method of detecting an HSV-1 expressing cell also employ vectors of the present invention that contain at least one transcriptional unit of a constitutive LAT promoter operatively linked to and controlling the transcription of a gene encoding a preselected protein.] Also, disclosed are kits for expressing in a mammalian cell a gene encoding a preselected protein, [useful for practicing the methods,] and mammalian cells containing the HSV-derived vectors.--.

IN THE CLAIMS:

Please cancel Claims 1-119 and 179-184, without prejudice, as being directed to designated claim Groups I, II, and III. Please cancel Claims 120-178, without prejudice, and add new Claims 185-202.

--185. (New) An HSV-1-derived vector, comprising a DNA having at least one nucleic acid sequence defining a functional LAT promoter, or operative fragment thereof; and further having a deletion in both copies of the HSV-1 LAT gene structural region, and a deletion in both copies of the HSV-1 ICP34.5 gene, such that functional RNA transcripts encoding the LAT gene product and encoding the ICP34.5 gene product cannot be detected within a mammalian cell hosting said vector.

186. (New) The HSV-1-derived vector of Claims 185, further comprising a functional HSV thymidine kinase gene.

187. (New) The HSV-derived vector of Claim 185, wherein said HSV-1-derived vector is derived from HSV-1 strain McKrae.

188. (New) The HSV-1-derived vector of Claim 187, wherein the HSV-1-derived vector is Prom Δ LAT Δ 34.5, Prom Δ LAT Δ 34.5-GFP, or a derivative of either of these.

189. (New) The HSV-1-derived vector of Claim 185, wherein the at least one transcriptional unit having a functional LAT Promoter sequence or operative fragment thereof is operatively linked to a nucleic acid encoding a preselected protein.

190. (New) The HSV-1-derived vector of Claim 189, wherein the preselected protein is a fluorescent or light-emitting protein or cytokine.

191. (New) The HSV-1-derived vector of Claim 190, wherein said fluorescent or light-emitting protein is a green fluorescent protein, yellow fluorescent protein, blue fluorescent protein, phycobiliprotein, luciferase, or apoaequorin.

192. (New) The HSV-1-derived vector of Claim 191, wherein the vector is Prom Δ LAT Δ 34.5-GFP or a derivative thereof.

193. (New) The HSV-1-derived vector of Claim 189, wherein the preselected protein is a protein toxic to cells expressing HSV.

194. (New) The HSV-1-derived vector of Claim 189, wherein the preselected protein is human interferon- γ , interleukin-2, interleukin-4, interleukin-6, interleukin-10, interleukin-12, granulocyte-macrophage colony stimulating factor, tumor necrosis factor- α , Fas ligand, human connexin-43, VP-16, or VP-22, or a fusion protein derived from any of these.

195. (New) A mammalian cell containing an HSV-1-derived vector selected from the group consisting of Prom Δ LAT Δ 34.5 and Prom Δ LAT Δ 34.5-GFP, or containing a derivative or unpackaged DNA of any of these.

196. (New) The mammalian cell of Claim 195, wherein said cell is a malignant cell.

197. (New) The mammalian cell of Claim 195, wherein said cell is a non-malignant cell.

198. (New) The mammalian cell of Claim 195, wherein said cell is a malignant cell derived from or is contained in a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, lymphoma, or carcinoma.

199. (New) The mammalian cell of Claim 195, wherein said mammalian cell is derived from or is contained in a human, non-human primate, mouse, rat, gerbil, hamster, or rabbit.

200. (New) A mammalian cell containing the HSV-1-derived vector of any of Claims 185, 186, 187, 189, 190, 191, 193, or 194, or unpackaged DNA thereof.

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202. (New) A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of any of Claims 185, 186, 187, 189, 190, 191, 193, or 194.--.